133. A humanized immunoglobulin according to any one of claims 119 to 130, which comprises two light chain/heavy chain dimers.

134. A humanized immunoglobulin according to any one of claims 119 through 130, which is substantially pure.

135. A pharmaceutical composition comprising a humanized immunoglobulin according to claim 134 in a pharmaceutically acceptable carrier.

Remarks

In view of the cancellation of all previously pending claims, it is respectfully submitted that the restriction requirement mailed February 21, 1997 is moot. Further, it is submitted that the replacement claims are sufficiently related that they can be examined in the same application. Applicants regret any inconvenience to the Examiner from the current request for entry of new claims; however, such is necessary in view of the early priority date of the present application, and the consequent loss of patent term that would result from presenting the current claims in a continuation application.

The rationale and support for the new claims are, briefly, as follows. Claims 111-114 are directed to methods of expressing humanized immunoglobulins from a cell. In claim 111, the cell was produced by a method similar to that defined in claim 99 of allowed case 08/487,200. In claim 112, the humanized immunoglobulin is defined similarly to the humanized antibody of claim 86 in allowed case 08/487,200. In claim 113, the humanized immunoglobulin is defined similarly to that of claim 4 of issued application USSN 08/477,728 (now US 5,585,089), although the present claims specify that binding affinity has a lower limit of about 10^8 M^{-1} and requires substitution of donor framework residues into the acceptor heavy chain. In claim 114, the humanized immunoglobulin is defined similarly to the humanized immunoglobulin of claim 3 of issued USSN 08/477,728; however, in

the present claim, CDRs are defined by the Kabat convention, and the binding affinity range is from 10^8-$10^{10}M^{-1}$ (see specification at e.g., pp. 25, lines 32-33). Claims 115-118 are directed to methods of producing a pharmaceutical composition (see specification at paragraph bridging pp. 71-72). In these claims, humanized immunoglobulins are defined analogously to the humanized immunoglobulins of claims 111-114 respectively. Claim 119 defines humanized immunoglobulins in the same manner as claim 113. Claim 120 is similar to issued claim 4 of USSN 08/477,728, except that the binding affinity range is from about 10^8-10^{10} M^{-1}. Claim 121 is similar to issued claim 3 in USSN 08/477,728 except that the binding affinity range is from about 10^8-10^{10} M^{-1}. Claim 122 is similar to issued claim 4 of USSN 08/477,728 except that the lower binding affinity is defined as 10^8 M^{-1} and the Kabat definition of CDRs is used. Claim 123 defines a humanized immunoglobulin as in present claim 114. The remaining claims are all dependent claims, and in general, parallel allowed or issued claims in related cases. Support for the substitution of at least 3 amino acids in claim 132 from the donor immunoglobulin framework is provided at specification p. 5, line 22.

Respectfully submitted,

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